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Challenging Occam's razor: An unusual combination of sarcoidosis and amyloidosis.

The value of CMR in infiltrative cardiomyopathies.

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Brief summary

There are only few cases in the literature of light-chain amyloidosis (AL) occurring in parallel to sarcoidosis. We present a patient with chronic sarcoidosis, heart failure and severe arrhythmia secondary to AL amyloidosis involvement. We highlight the value of cardiovascular magnetic resonance to discriminate between different patterns of myocardial infiltration and identify the diagnosis of cardiac amyloidosis.

Abstract

We describe the case of a 66-year old woman with the extremely rare combination of sarcoidosis-amyloidosis (light-chain) and the important role of cardiovascular magnetic resonance imaging to differentiate between these two infiltrative diseases. Myocardial characterization with T1 mapping can improve disease detection especially in overlap cases and possibly obviate the need for cardiac biopsy.

Introduction

With the use of cardiovascular magnetic resonance imaging (CMR) and accurate myocardial tissue characterisation, the aetiology of a variety of cardiomyopathies can be differentiated, potentially obviating the need for invasive testing and myocardial tissue biopsy.

Sarcoidosis and amyloidosis both represent systemic infiltrative diseases associated with non-caseating granuloma formation and amyloid deposition respectively, in a range of tissues and organs. Although cardiac involvement carries a poor prognosis in both systemic amyloidosis and sarcoidosis, specific therapeutic options exist for both pathologies and hence accurate identification of the aetiology of the cardiomyopathy is crucial. Late gadolinium enhancement (LGE) CMR is useful for the detection of cardiac infiltration, but LGE patterns are not always typical and often overlap making the interpretation challenging. Myocardial characterization with T1 mapping can improve disease detection especially in overlap cases.

Case Presentation

A 66-year-old woman with long standing active multi-system sarcoidosis on corticosteroid and methotrexate therapy presented with cardiac chest pain, non-sustained ventricular tachycardia and mildly elevated troponin. Inpatient coronary angiography showed no obstructive coronary artery disease. She was referred to our institution for consideration of an implantable cardioverter defibrillator (ICD). A CMR was requested prior to the ICD to assess for any cardiac sarcoidosis involvement. Anatomical and functional cine CMR images showed concentric hypertrophy of the left ventricle (LV) (maximum thickness 17mm), normal ejection fraction and mildly dilated atria. Long axis function was reduced for both ventricles (MAPSE 7mm, TAPSE 10mm) in keeping with restrictive physiology. In the late

phase after gadolinium it proved difficult to null the myocardium (Figure 1) but there was a suggestion of heterogeneity in the signal intensity across the myocardium with a prominent and dense mid-wall enhancement in the apical septum and basal inferolateral wall. At this stage (30 minutes after Gadolinium injection) post-contrast T1 mapping using a high resolution 4(1)3(1)2 MOLLI prototype sequence (Siemens WIP 448B) as shown in Figure 2 was performed on a 1.5T scanner (Magnetom Avanto^{fit}, Siemens Healthcare, Erlangen, Germany). This interestingly confirmed abnormal gadolinium kinetics; septal myocardial T1=379ms, blood T1=409ms. In particular, the myocardial post-contrast T1 value was lower than the post-contrast blood value. This reversed pattern (post-contrast T1 blood>myocardium) is abnormal and to date has only been described in the amyloid population¹. As T1 mapping was not part of the routine protocol but was requested upon the finding of an unusual LGE pattern, there were no native T1 values to allow calculation of ECV.

Based on the findings of T1 mapping as well as the difficulty to null the myocardium on LGE images, a diagnosis of cardiac amyloid in a patient with known systemic sarcoidosis was made and further tests to investigate this were organised.

The patient underwent (99m) Tc-3,3-diphosphono-1,2-propanodicarboxylic acid ((99m)Tc-DPD) scanning and 123I-labeled serum amyloid P component (SAP) scintigraphy. The DPD report was negative, , excluding transthyretin based disease². The SAP report was positive for a large amyloid load within the liver spleen and kidneys. The absence of heart uptake might be explained by the massive accumulation of the tracer in the visceral organs leaving no significant amount available for the heart or by the lack of fenestrated endothelium in the myocardium. Overall the technique has a lower diagnostic performance for the heart³. Serum biochemical investigations showed a lambda light chain in excess of 240mg/L (normal range 5.7-26.3mg/L). Fat pad aspirate biopsy showed the presence of amyloid by the staining of amorphous material with Congo red (Figures S1-S3). The diagnosis of AL amyloidosis with evidence of lambda light chain secreting plasma cell dyscrasia was reached and chemotherapy was initiated.

Discussion

The combination of sarcoidosis and amyloidosis is extremely rare and has only been described in seven cases (5 cases AA and 2 cases AL type) in the literature previously, all following myocardial biopsy, heart transplantation or autopsy⁴.

It has been argued that the sarcoidosis-related inflammatory process is implicated in the pathogenesis of AA amyloidosis. Long-standing inflammatory diseases are associated with increased concentrations of an acute phase reactant—serum amyloid A which is a precursor of amyloid AA protein. However, AA amyloidosis shows minimal involvement of the myocardium.

AL amyloidosis on the other hand is associated with plasma cell dyscrasias and shows extensive deposition in the heart. Even though the co-existence of AA amyloidosis and active sarcoidosis has been reported in 5 cases the relationship between cardiac AL amyloidosis and active systemic sarcoidosis as in our case is less well understood.

Two prior reports describe co-existence of cardiac sarcoidosis and AL amyloidosis, in the presence of a plasma cell dyscrasia⁴.

This is in keeping with a recent meta-analysis that has shown a significant (though moderate) association between sarcoidosis and malignancy, including myeloma, likely mediated via chronic inflammation or immune system derangement⁵.

In our case MOLLI T1 mapping was helpful to confirm the initial suspicion raised by the conventional CMR of an uncommon combination of sarcoidosis and amyloidosis involvement prompting for further invasive investigations.

Conclusion

To our knowledge, this is the first case reported in the literature where CMR was instrumental in the correct identification of cardiac amyloidosis in the setting of systemic sarcoidosis and T1 mapping was used for confirmation. The most likely causes of cardiac infiltration in our patient would have been active sarcoidosis or a sarcoidosis-related AA amyloidosis. However, a rarer combination was identified with AL amyloidosis and active sarcoidosis, challenging Occam's principle.

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Figure 1. Panel showing LGE images of the heart showing the difficulty in nulling myocardium at different inversion times and time intervals and the abnormal gadolinium kinetics.

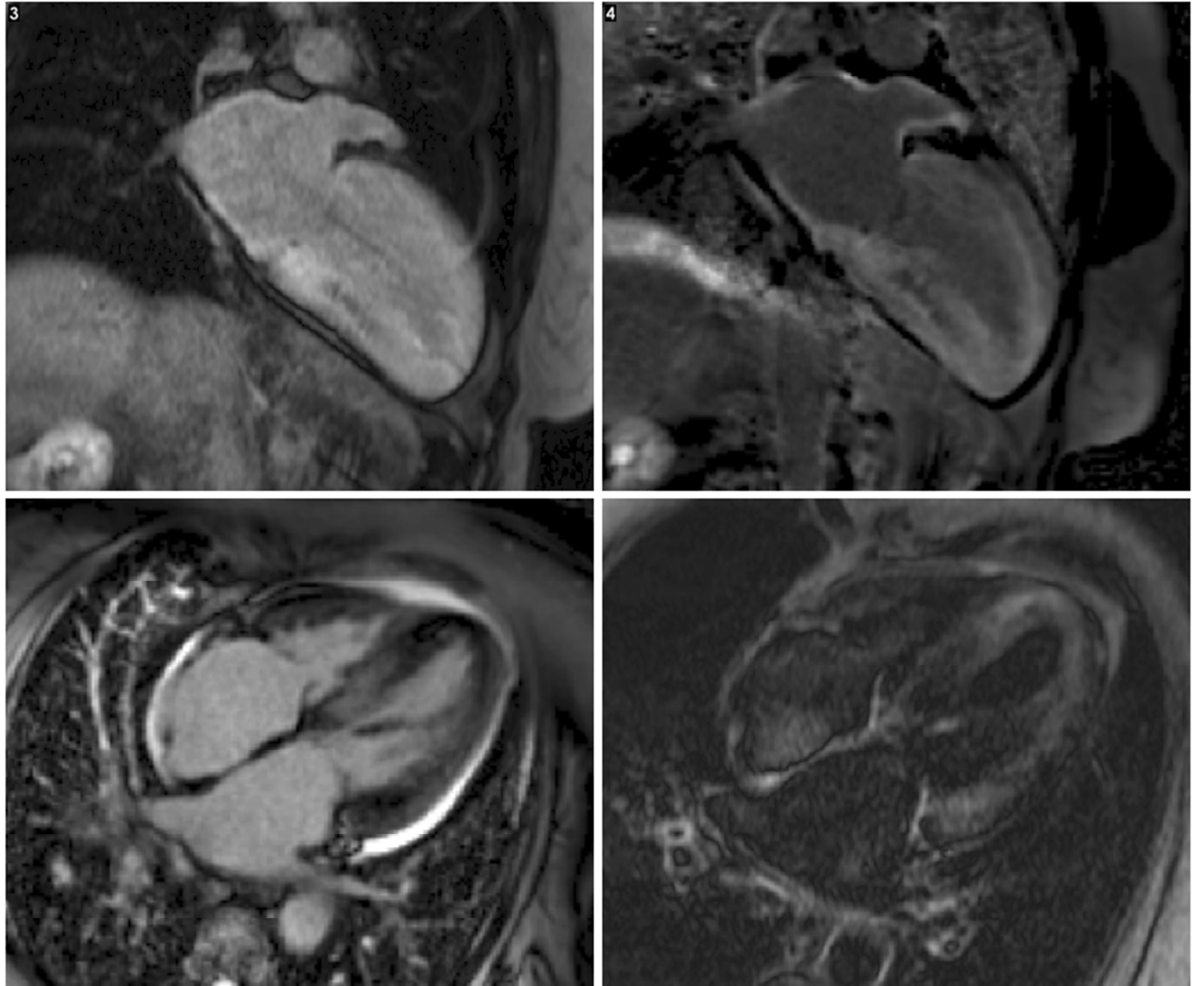


Figure 2. Panel A showing 30 minutes post-contrast myocardial T1 value being lower than post-contrast blood T1 (panel B). This is paradoxical so early after injection and only been reported in amyloid. Hence the suspicion of amyloid was raised in this patient and further invasive investigations undertaken which confirmed amyloid. T1 maps analysed by Circle CVI⁴², Calgary, Canada

